

3/10/2003

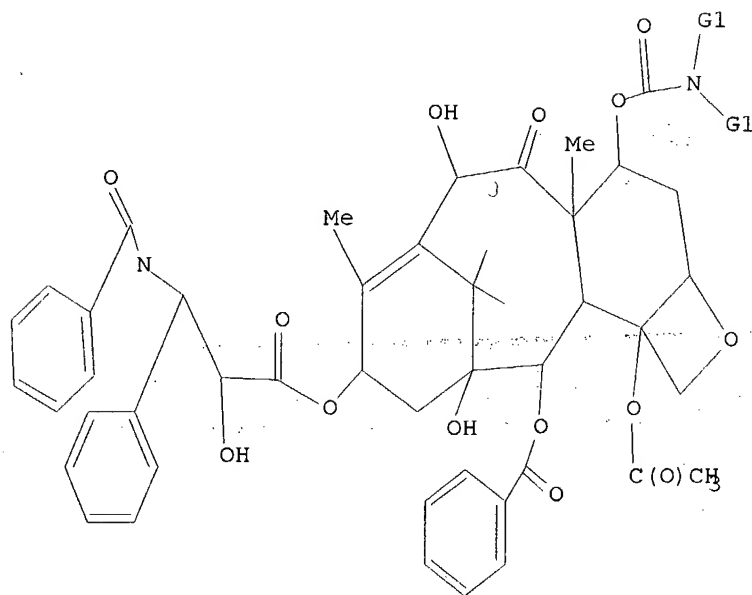
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L3 STRUCTURE UPLOADED

=> d 13

L3 HAS NO ANSWERS

L3 STR



G1 Cb,Cy,Hy,Ak,Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu,Ph,H

Structure attributes must be viewed using STN Express query preparation.

=> s 13 sss full

FULL SEARCH INITIATED 17:20:42 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 210 TO ITERATE

100.0% PROCESSED 210 ITERATIONS
SEARCH TIME: 00.00.01

0 ANSWERS

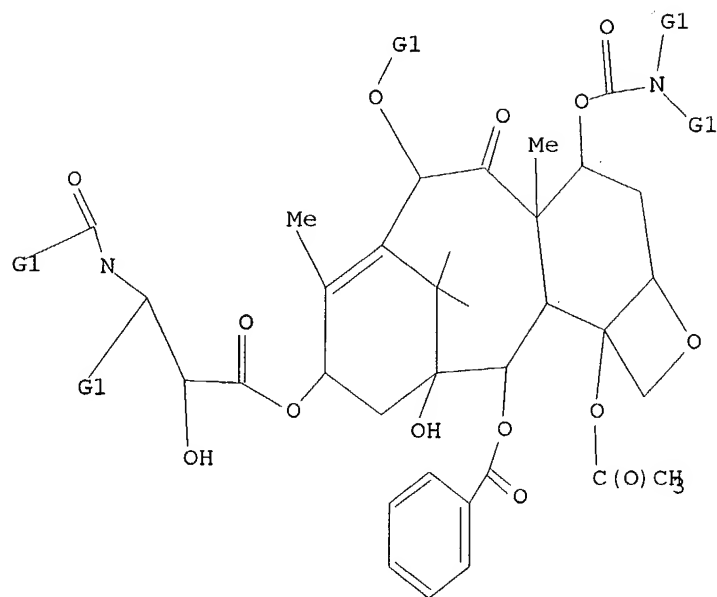
L4 0 SEA SSS FUL L3

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Uploading taxol.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS
L1 STR



G1 Cb,Cy,Hy,Ak,Me,Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu,Ph,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 17:25:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 248 TO ITERATE

100.0% PROCESSED 248 ITERATIONS

27 ANSWERS

> s 12

L3 12 L2

> d 13 1-12 ibib abs hitstr

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:640738 CAPLUS

DOCUMENT NUMBER: 131:267037

TITLE: Water soluble paclitaxel derivatives for treatment of tumors

INVENTOR(S): Li, Chun; Wallace, Sidney; Yu, Dong-fang; Yang, David

PATENT ASSIGNEE(S): Pg-Txl Company, L.P., USA

SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949901	A1	19991007	WO 1999-US6870	19990330
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9934556	A1	19991018	AU 1999-34556	19990330
EP 1028756	A1	20000823	EP 1999-916188	19990330
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: US 1998-50662 A2 19980330
WO 1999-US6870 W 19990330

AB Disclosed are water sol. compns. of paclitaxel and docetaxel formed by conjugating the paclitaxel or docetaxel to a water sol. polymer such as poly-glutamic acid, poly-aspartic acid or poly-lysine. Also disclosed

are methods of using the compns. for treatment of tumors, auto-immune disorders such as rheumatoid arthritis. Other embodiments include the coating of implantable stents for prevention of restenosis. Glutamic acid-paclitaxel copolymer (I) was prepd. by the reaction of polyglutamic acid with paclitaxel. Water sol. I had antitumor activity against

mammary carcinoma and mammary ovarian carcinoma and was more effective than paclitaxel on equiv. mg paclitaxel basis.

IT 245322-09-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(water sol. paclitaxel derivs. for treatment of tumors)

RN 245322-09-2 CAPLUS

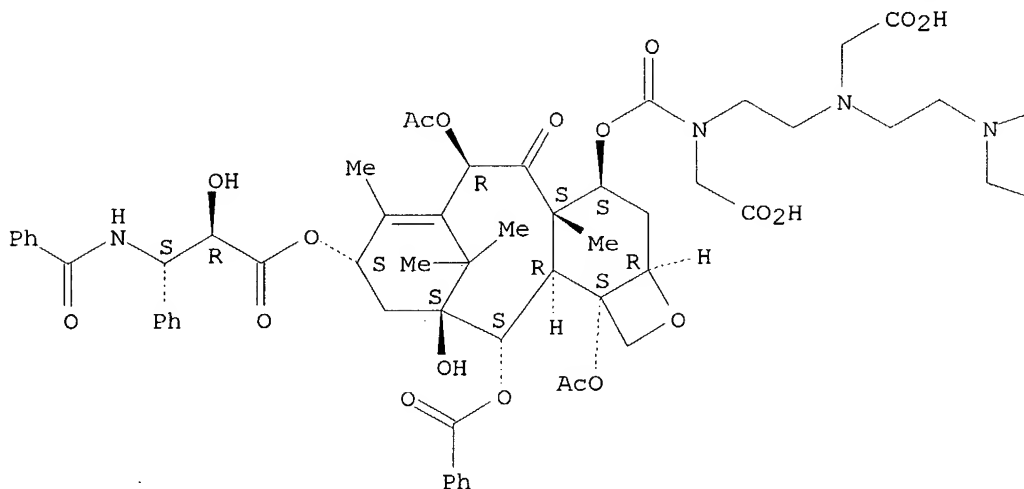
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

(2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-

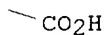
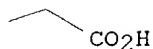
4-[[[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl](carboxymethyl)amino]carbonyloxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4
REFERENCE (S): (1) Brem; US 5626862 A 1997 CAPLUS
(2) Butterfield; US 5730968 A 1998 CAPLUS
(3) Li, C; Pharmaceutical Research 1996, V13(9), PS-368
(4) Mongelli; US 5473055 A 1995 CAPLUS

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282391 CAPLUS
DOCUMENT NUMBER: 130:352485
TITLE: Synthetic studies of sialo-glycoconjugates
AUTHOR(S): Takahashi, T.; Tsukamoto, H.; Kurosaki, M.; Yamada, H.
CORPORATE SOURCE: Department of Chemical Engineering, Tokyo Institute of Technology, Tokyo, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1997), 39th, 49-54
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai

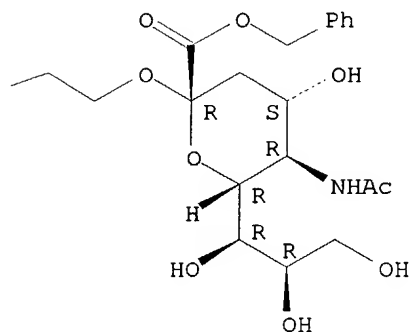
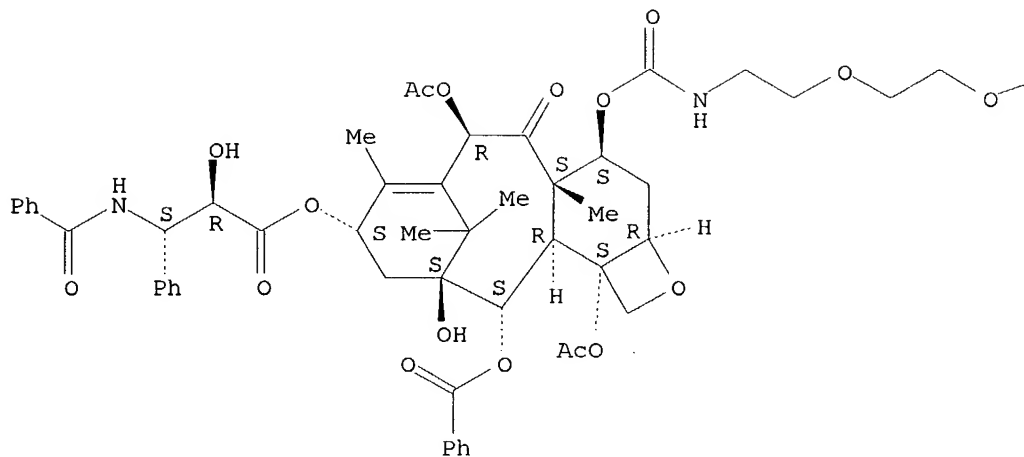
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB N-Acetyl neuraminic acid (Neu5Ac) is incorporated at the nonreducing terminal position of glycoconjugates which are found in cell membranes and in nervous systems of various living organisms. These sialyl conjugates play an essential role in biol. mol. recognition processes, such as cell adhesion and differentiation phenomena. For the elucidation of these biol. properties and functions, the supply of natural and nonnatural sialyl conjugates with a definite structures is indispensable. The ulosonic acids such as Neu5Ac, KDO, and KDN have the .alpha.-ketoacid moieties which exist in a 6-membered cyclic hemiacetal form. To establish a general synthetic method for monosaccharides contg. the .alpha.-ketoacid structures, we examd. the synthesis of Neu5Ac utilizing alkylation of 2-alkoxy-2-cyanoacetate [I; R = Me3CSiMe2 (TBS)], an acylanion equiv. of alkyl glyoxylate, with bromide (II; R = Br; MOM = CH2OMe) derived from the com. available D-glycero-D-gulo-heptose-1,4-lactone, to give II [R = C(CN)(OTBS)CO2CMe3]. We also examd. the syntheses of KDO and KDN based on alkylation of 2-alkoxy-2-cyanoacetate [I; R = 1-ethoxyethyl (EE)] with the sugar-derived iodide (III; R = iodo) and triflate (IV; R = CF3SO3) to give III [R = C(CN)(OEE)CO2CMe3] and IV [R = C(CN)(OEE)CO2CMe3], resp. One of the most difficult problem in the synthesis of sialyl conjugate is the stereoselective glycosidation of sialic acid with .alpha.-glycosidic linkage. First, we examd. a new method for .alpha.-glycoside formation of sialyl conjugate utilizing the concept of "long-range participation". When 2-methylthioethyl ester was introduced into the carboxylic acid in the sialic acid as neighboring group (V) and DME was used as solvent, highly .alpha.-selective glycosylation was achieved in moderate yields. To improve the yields, we examd. alkylation of 2-alkoxy-2-phenylthioacetate (VI; R = H) 34 with allyl bromide (Q-Br) 36 to form an intermediate (VI; R = Q) followed by an intamol. glycosylation to an intermediate (VII). Phenylthio-group serves as not only a stabilizer of an enolate in the alkylation but also a leaving group in the glycosylation. This method are underway in our lab.

IT 202194-43-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of N-acetylneuraminic acid, KDN, KDO, and sialo-glycoconjugates via alkylation of alkoxyacyanoacetate with pentahydroxyheptenyl bromide and hexahydroxyheptyl triflate)

RN 202194-43-2 CAPLUS
 CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-[[[[[(2aR, 4aS, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6,12b-bis(acetyloxy)-9-[(2R, 3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, phenylmethyl ester (9CI)

(CA INDEX NAME)



IT 225235-44-9P

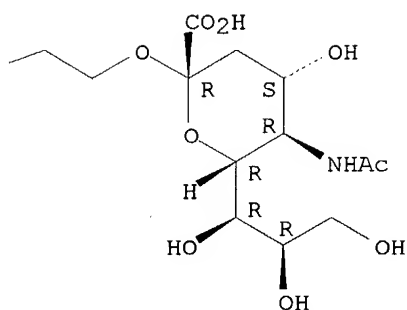
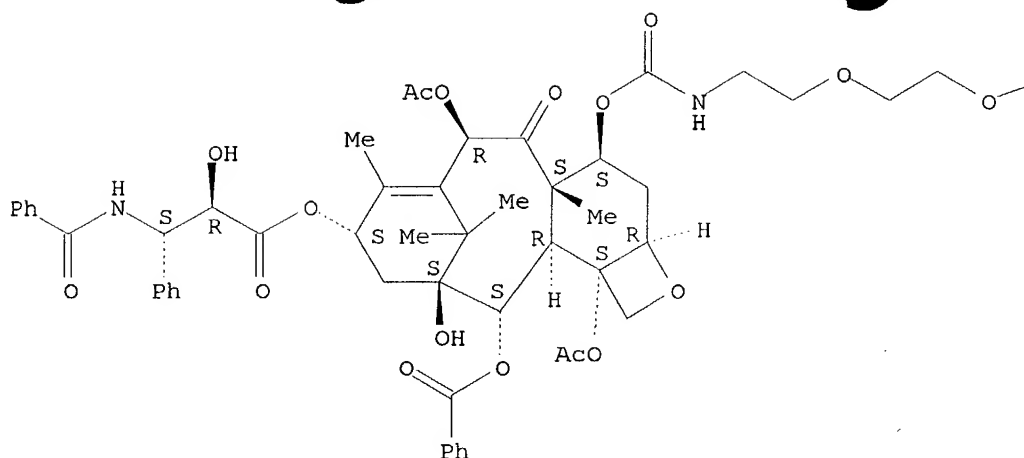
RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of N-acetylneuraminic acid, KDN, KDO, and
 sialo-glycoconjugates
 via alkylation of alkoxycyanoacetate with pentahydroxyheptenyl bromide
 and hexahydroxyheptyl triflate)

RN 225235-44-9 CAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-

[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L3 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:64977 CAPLUS

DOCUMENT NUMBER: 130:119580

TITLE: Identification of molecular targets of drugs or toxins

INVENTOR(S): Makowski, Lee; Makowski, Diane R.; Sanganeer, Hitesh J.

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902733	A1	19990121	WO 1998-US14082	19980707
W: CN, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 990051	A1	20000405	EP 1998-945752	19980707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-51780	19970707
			US 1997-51781	19970707

AB Identification of the mol. targets of a drug or toxin is the first step in

understanding how the drug or toxin works, and important advance in learning how to improve a drug or assess the risks due to a toxin. The primary action of a drug usually involves binding to a protein; secondary actions may express themselves in the form of side effects and in some cases may be due to binding to other proteins. Consequently, it is useful

to identify all physiol. relevant sites of action of a drug or toxin. A simple method for obtaining a list of the potential targets of a drug, toxin or other biol. active substance (referred to collectively as ligands) involves a multistep process. The first step is screening a protein or peptide library to identify library members that exhibit high affinity for a particular ligand. The second step involves searching of sequence data bases for proteins that contain the sequences of the

library

members shown to have high affinity for the ligand. The proteins thus identified constitute a list of potential targets for the ligand. If random peptide libraries have been used, the position of identified consensus sequences within the identified protein constitutes an identification of the potential ligand binding site on the target.

IT 219950-34-2P 219950-36-4P 219950-38-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(drug or toxin mol. target identification)

RN 219950-34-2 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

4-[[[4-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-

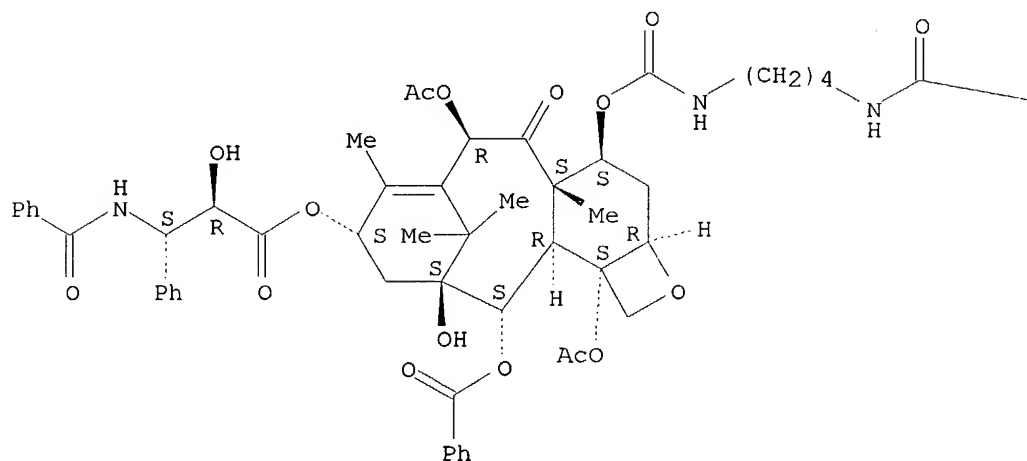
oxopentyl]amino]butyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-

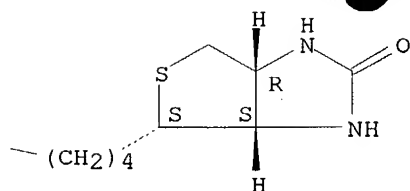
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-

cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





RN 219950-36-4 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

(2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-

4-[[[6-[[5-[(3aS, 4S, 6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-

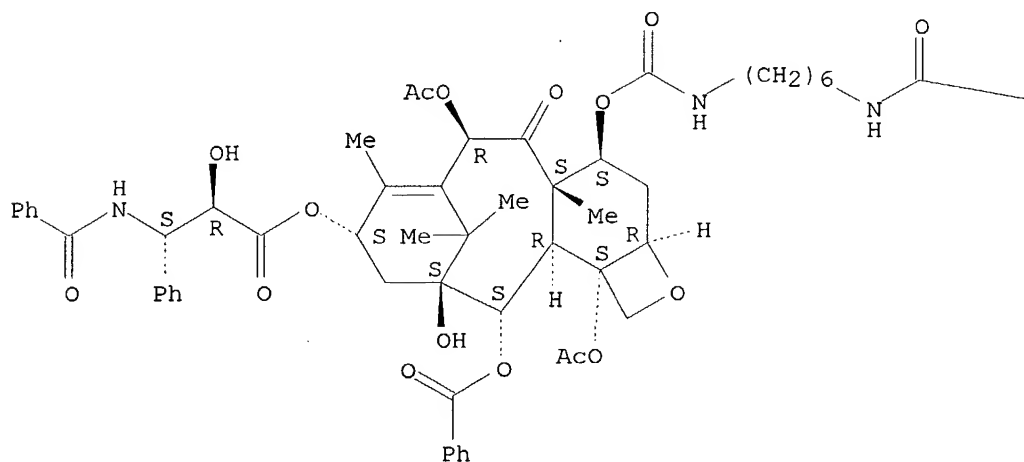
oxopentyl]amino]hexyl]amino]carbonyloxy]-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-

dodecahydro-11-hydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-

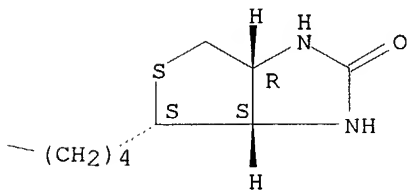
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (.alpha.R, .beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 219950-38-6 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

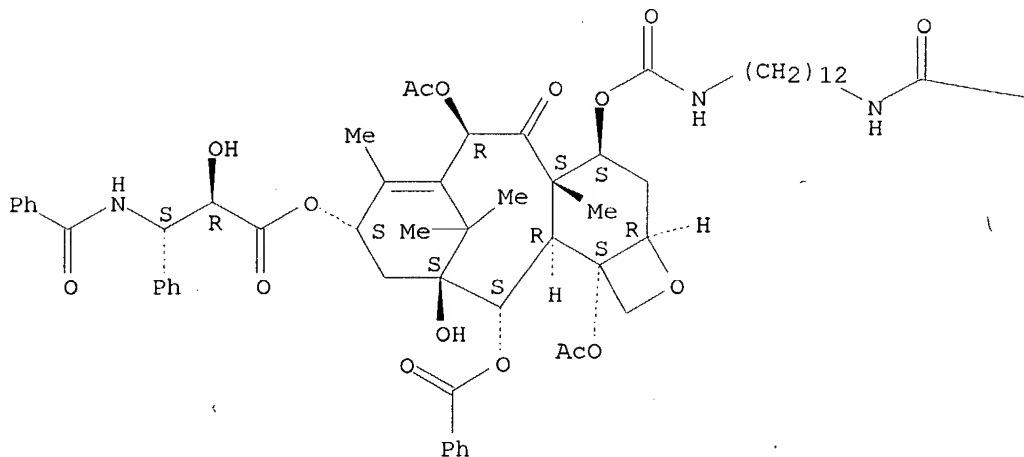
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4-[[[12-[[5-[(3aS, 4S, 6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-

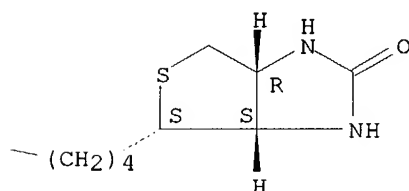
1-oxopentyl]amino]dodecyl]amino]carbonyl]oxy]-
 2a,3,4,4a,5,6,9,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
 ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

6

REFERENCE(S):

- (1) Bruno, J; Biochemical and Biophysical Research Communications 1997, V236, P344 CAPLUS
 - (2) Cwirla, S; Peptides on phage: a vast library of peptides for identifying ligands 1990, V87, P6378 CAPLUS
 - (3) Devlin, J; Random Peptide Libraries: A source of specific protein binding molecules 1990, V249, P404 CAPLUS
 - (4) Dower; US 5432018 A 1995 CAPLUS
 - (5) McCoy; US 5635182 A 1997 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:48806 CAPLUS

DOCUMENT NUMBER: 128:140940

TITLE: Design and synthesis of a water-soluble taxol analog: taxol-sialyl conjugate

AUTHOR(S): Takahashi, Takashi; Tsukamoto, Hirokazu; Yamada, Haruo

CORPORATE SOURCE: Department of Chemical Engineering, Tokyo Institute of Technology, Tokyo, 152, Japan

SOURCE: Bioorg. Med. Chem. Lett. (1998) 8(1), 113-116
CODEN: BMCLE8; ISSN: 0960-8941
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glycosidation, using the methylthio deriv. of N-acetylneuraminic acid, of a linker alc. in DME with "long-range participation" produced the .alpha.-glycosyl linkage with high stereoselectivity. The .alpha.-linked sialic acid was introduced in taxol without protection of the alc. functionality in sialic acid. The taxol-sialyl conjugate was tested for water soly., microtubule binding and cytotoxicity assay.

IT 202194-38-5P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and prepn. of a water-sol. taxol analog)

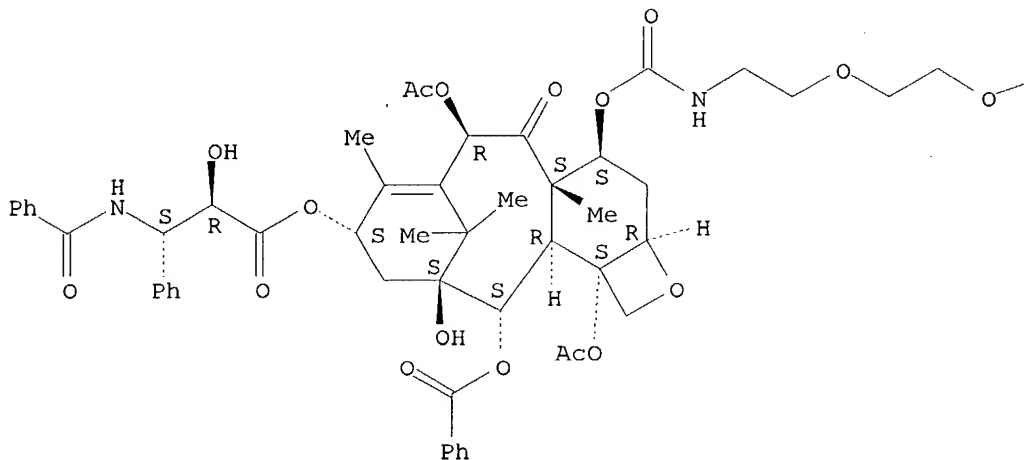
RN 202194-38-5 CAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-

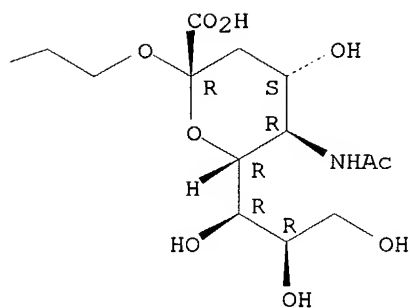
[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



● Na



IT 202194-43-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(design and prepn. of a water-sol. taxol analog)

RN 202194-43-2 CAPLUS

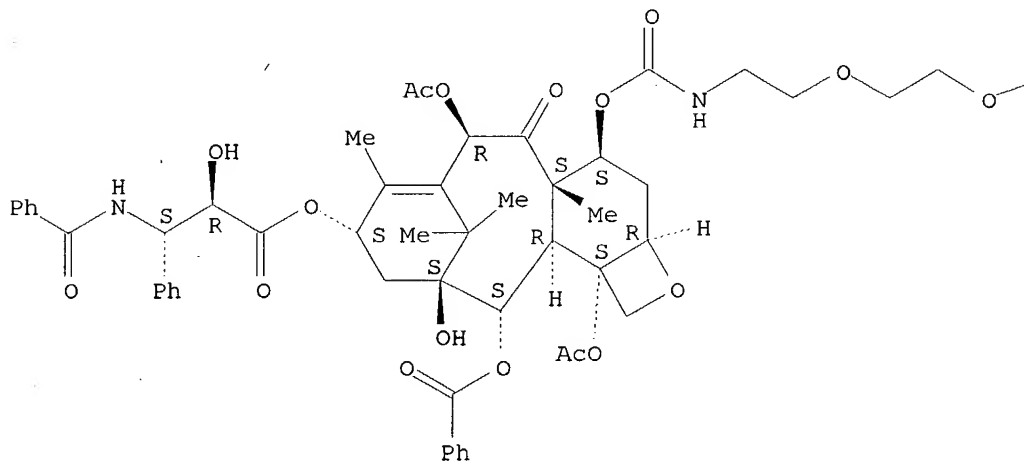
CN .alpha.-Neuraminic acid, N-acetyl-2-O-[2-[2-[2-

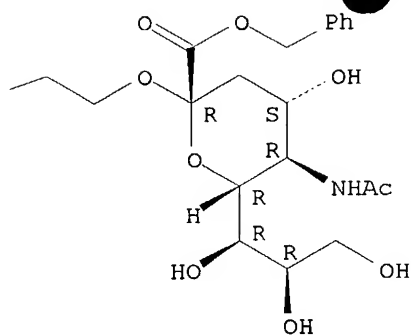
[[[(2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis (acetyloxy)-9-[(2R, 3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-11-hydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-4-yl]oxy]carbonyl]amino]ethoxy]ethoxy]ethyl]-, phenylmethyl ester (9CI)

(CA

INDEX NAME)

Absolute stereochemistry.





L3 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:231372 CAPLUS

DOCUMENT NUMBER: 126:308799

TITLE: High-molecular-weight polymer-based prodrugs

INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna

PATENT ASSIGNEE(S): Enzon, Inc., USA

SOURCE: U.S., 11 pp. Cont. of U.S. Ser. No. 140,346, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 12

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5614549	A	19970325	US 1995-380873	19950130
US 5880131	A	19990309	US 1995-537207	19950929
CA 2208841	AA	19960808	CA 1996-2208841	19960130
WO 9623794	A1	19960808	WO 1996-US1459	19960130
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
AU 9649133	A1	19960821	AU 1996-49133	19960130
AU 705147	B2	19990513		
EP 807115	A1	19971119	EP 1996-905345	19960130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 10513187	T2	19981215	JP 1996-523755	19960130
US 5840900	A	19981124	US 1996-700269	19960820
US 5965566	A	19991012	US 1997-914927	19970820
US 6127355	A	20001003	US 1999-277230	19990326
PRIORITY APPLN. INFO.:			US 1992-934131	B2 19920821
			US 1993-28743	B2 19930309
			US 1993-140346	B2 19931020
			US 1995-380873	A2 19950130
			US 1995-537207	A 19950929
			WO 1996-US1459	W 19960130
			US 1996-700269	A2 19960820
			US 1997-914927	A1 19970820

OTHER SOURCE(S): MARPAT 126:308799

AB Water-sol. prodrugs comprise hydrolyzable linkages between a polymer portion and a biol. active nucleophile, preferably taxoids. PEG 40,000 dicarboxylic acid bis(taxol-2'-diester) was prepd. and injected to P388/0 murine lymphoid neoplasm-infected mice to det. the ability of the prodrug

to increase the life span of the mice.

IT 161742-57-0P

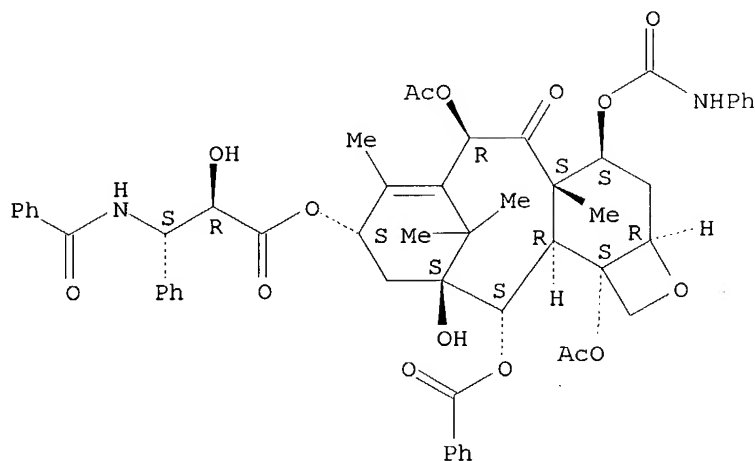
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of high-mol.-wt. polymer-based water-sol. prodrugs)

RN 161742-57-0 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-

[[(phenylamino)carbonyloxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-
9-yl ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.b
eta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L3 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:148858 CAPLUS

DOCUMENT NUMBER: 126:162276

TITLE: Androgenic receptor-binding phenylthiohydantoins for
diagnosis and treatment of prostate cancer

INVENTOR(S): Sovak, Milos; Bressi, Jerome C.; Douglass, James
Gordon, III; Campion, Brian; Wrasidlo, Wolfgang

PATENT ASSIGNEE(S): Biophysica Foundation, USA; Sovak, Milos; Bressi,
Jerome C.; Douglass, James Gordon, III; Campion,
Brian; Wrasidlo, Wolfgang

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

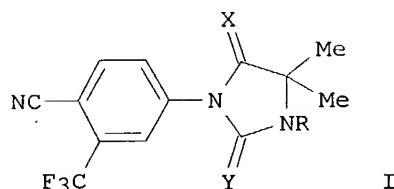
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

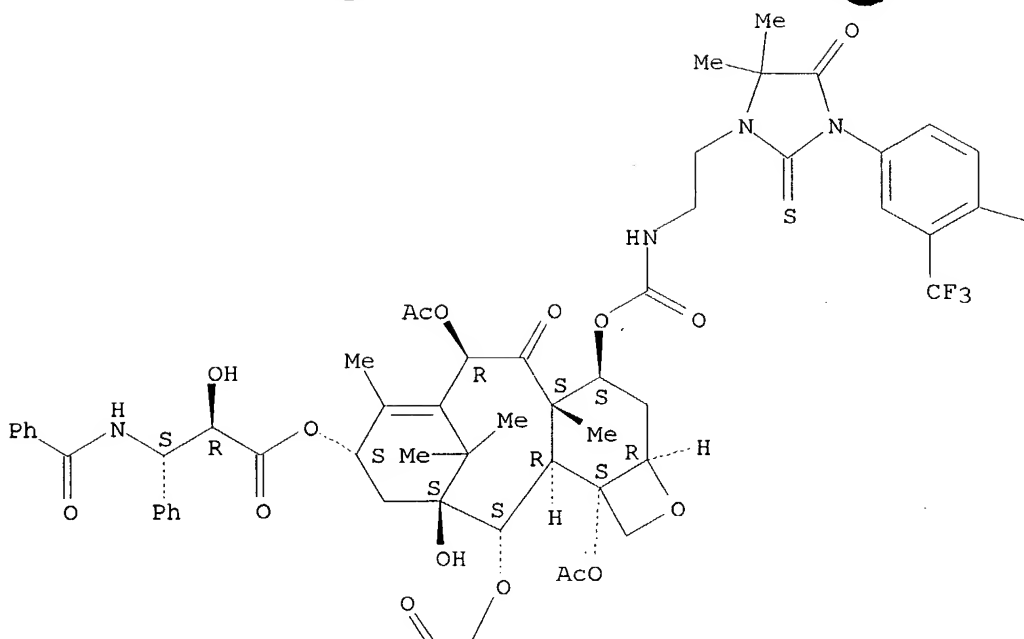
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700071	A1	19970103	WO 1996-US10286	19960613
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA			
US 5656651	A	19970812	US 1995-491130	19950616
CA 2225484	AA	19970103	CA 1996-2225484	19960613

AU 9663329 1 19970115 AU 1996-6337 19960613
 AU 712609 2 19991111
 EP 854716 A1 19980729 EP 1996-922463 19960613
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 JP 10510845 T2 19981020 JP 1996-503330 19960613
 PRIORITY APPLN. INFO.: US 1995-491130 19950616
 WO 1996-US10286 19960613
 OTHER SOURCE(S): MARPAT 126:162276
 GI



AB Substituted phenylthiohydantoin (I; X, Y = O, S, NH; R = aliph., aryl,
 or aralkyl linking group) are provided for use in detecting tumor cells
 having androgenic receptors. These compds. can be used for specific
 targeting to the androgenic receptor-contg. cells of cytostatic and/or
 cytotoxic agents, heavy or light radioactive or radiopaque atoms, etc.
 for detection and treatment of cancer cells contg. androgenic receptors (e.g.
 prostate cancer cells). Thus, cycloaddn. of 2-[[[N-(tert-
 butoxycarbonyl)amino]ethyl]amino]-2-cyanopropane to 2-trifluoromethyl-4-
 isothiocyantobenzonitrile produced I (X = NH, Y = S, R =
 CH₂CH₂NHCO₂Bu-t)
 (BP-136), which was converted to the unprotected aminoethyl deriv.
 (BP-138) with HCl. BP-138 was conjugated with
 2'-(triethylsilyloxy)-7-(p-
 nitrophenoxycarbonyl)paclitaxel (prepn. given) to produce a targeted
 cytotoxic agent.
 IT **186040-53-9P**
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (androgenic receptor-binding phenylthiohydantoin for diagnosis and
 treatment of prostate cancer)
 RN 186040-53-9 CAPLUS
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[2-[3-[4-cyano-3-
 (trifluoromethyl)phenyl]-5,5-dimethyl-4-oxo-2-thioxo-1-
 imidazolidinyl]ethyl]amino]carbonyloxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
 dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-
 [2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,
 12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.



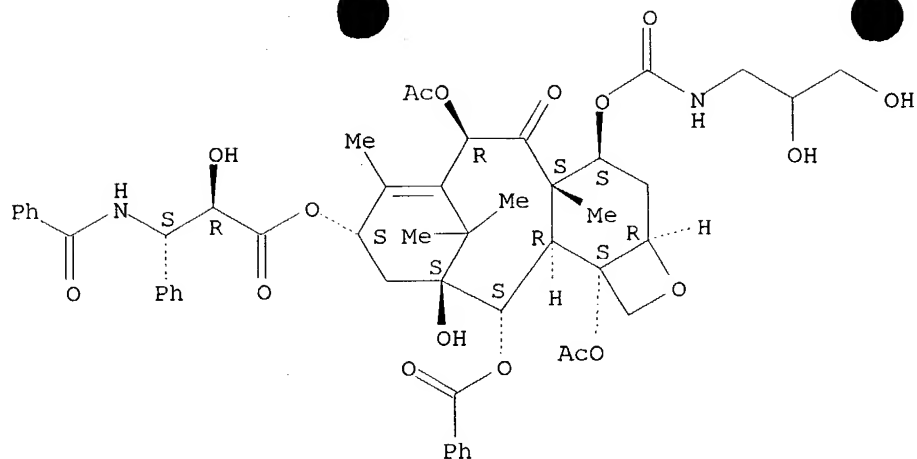
CN



L3 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1997:105187 CAPLUS
 DOCUMENT NUMBER: 126:113164
 TITLE: Novel taxoids as antiproliferative agents
 INVENTOR(S): Sovak, Milos; Douglass, James G.; Bressi, Jerome C.;
 Seligson, Allen
 PATENT ASSIGNEE(S): Biophysics Foundation, USA; Sovak, Milos; Douglass,
 James G.; Bressi, Jerome C.; Seligson, Allen
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	IND	DATE	APPLICATION	DATE
WO 9638138	A1	19961205	WO 1996-US8245	19960531
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5801191	A	19980901	US 1995-457674	19950601
CA 2222299	AA	19961205	CA 1996-2222299	19960531
AU 9659622	A1	19961218	AU 1996-59622	19960531
AU 713097	B2	19991125		
EP 833628	A1	19980408	EP 1996-916900	19960531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10509461	T2	19980914	JP 1996-536740	19960531
PRIORITY APPLN. INFO.:			US 1995-457674	19950601
			WO 1996-US8245	19960531
OTHER SOURCE(S): MARPAT 126:113164				
AB	Novel taxoids are provided having enhanced water soly. and/or improved pharmacol. properties as compared to paclitaxel. The subject taxoids comprise a functional group attached to a paclitaxel at the C-2' and/or C-7 position by a linking group. Functional groups present in the subject taxoids may be hydrophilic chains, groups capable of in vivo conversion to hydrophilic chains, targeting moieties capable of specifically binding with cellular receptors and water sol. polymers of at least 5 kD. The subject taxoids find use in the treatment of hosts suffering from a cellular proliferative disease.			
IT	186032-89-3P, BP 187 186040-53-9P, BP 196 186040-55-1P, BP 184 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (novel taxoids as antiproliferative agents)			
RN	186032-89-3 CAPLUS			
CN	Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(2,3-dihydroxypropyl)amino]carbonyloxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-[partial]- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.



RN 186040-53-9 CAPLUS

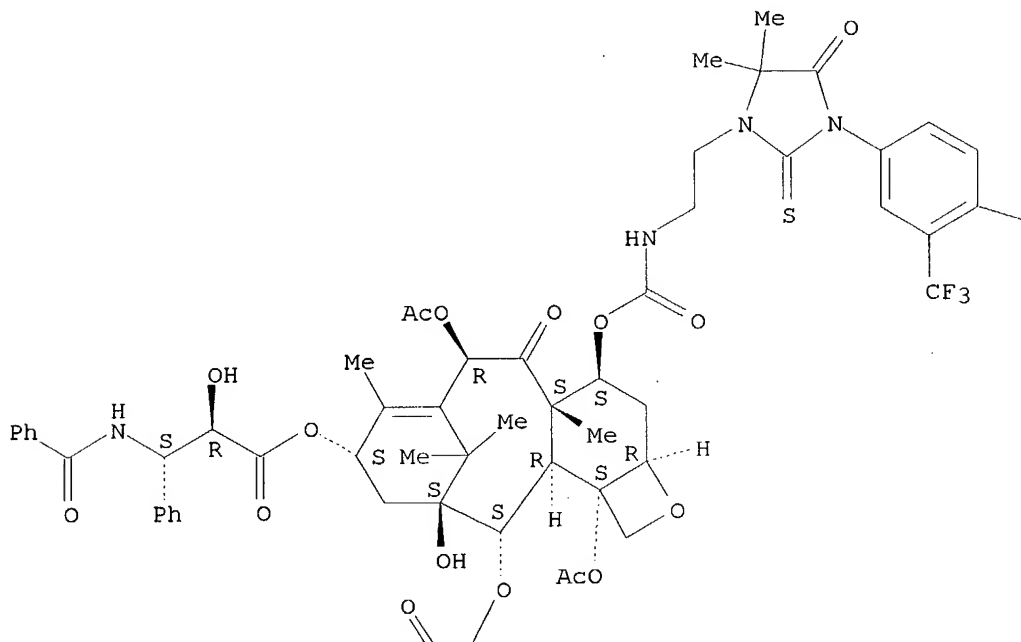
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[2-[3-[4-cyano-3-(
(trifluoromethyl)phenyl]-5,5-dimethyl-4-oxo-2-thioxo-1-

imidazolidinyl]ethyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,
12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



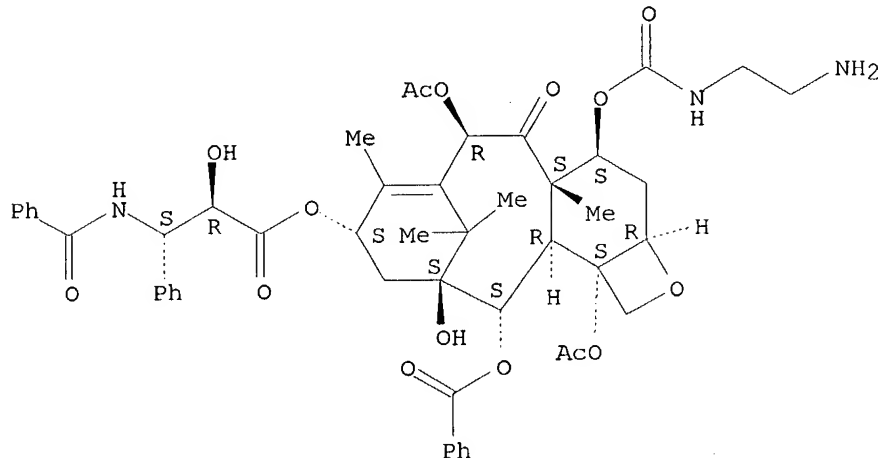
CN

PAGE 2-A



RN 186040-55-1 CAPLUS
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
 6,12b-bis(acetyloxy)-4-[[[(2-aminoethyl)amino]carbonyl]oxy]-12-
 (benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-
 4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-
 9-yl ester,
 [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.b
 eta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX
 NAME)

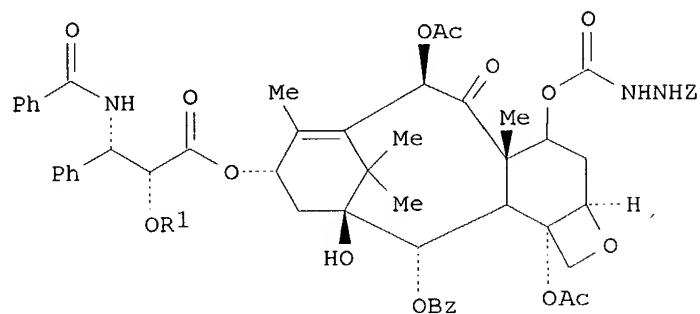
Absolute stereochemistry.



L3 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1996:537798 CAPLUS
 DOCUMENT NUMBER: 125:196059
 TITLE: Taxol-7-carbazates with improved water-solubility
 and/or enhanced therapeutic activity
 INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
 PATENT ASSIGNEE(S): Enzon, Inc., USA
 SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 140, 346,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUN: 12
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5547981	A	19960820	US 1994-198194	19940217
PRIORITY APPLN. INFO.:			US 1993-28743	B2 19930309
			US 1993-140346	B2 19931020
OTHER SOURCE(S):			CASREACT 125:196059; MARPAT 125:196059	
GI				



AB Disclosed are 7-substituted taxoid derivs., in particular taxol-7-carbazates which have improved water-soly. and/or enhanced therapeutic activity and methods of making the same. The preferred taxoid

derivs. have the formula I, wherein Z is H or (C:Y)nXR, Y = O or S; X = CH2 or O; n = zero or a pos. integer, preferably one; with the proviso that when n = 0, X = CH2; R = C1-C4-alkyl, haloalkyl, carboxyalkyl, thioalkyl, sulfonylalkyl, Ph, hydroxyphenyl, aminophenyl, carboxyphenyl,

a polyalkyleneoxide homopolymer or water sol. polyalkyleneoxide contg. copolymer, having a mol. wt. of from about 1,000 to about 20,000; R1 = H or (C:O)CH2WR2; W = O, N--L, S or SO2; L = H, C1-C4-alkyl or Ph; and R2

= C1-C4-alkyl, Ph or a polyalkyleneoxide homopolymer or water sol. polyalkyleneoxide contg. copolymer, having a mol. wt. of from about 1,000 to about 20,000. I are prepd. by reacting taxol first with carbonyl diimidazole, bis-succinimidyl carbonate, phosgene or p-nitrophenyl chloroformate, followed by acetic hydrazide, t-Bu carbazate, polyethylene glycol hydrazide or carbazate. I are useful in the treatment of neoplastic disease, tumor burden, metastasis of neoplasms and recurrences of tumor and neoplastic growths.

IT **180965-73-5DP**, 7-(Carboxyhydrazidocarbonyl)taxol, polyethylene glycol deriv. ester **180965-75-7P** **180965-76-8P**, 7-(Acetohydrazidocarbonyl)taxol

RL: BAC (Biological activity or effector, except adverse); IMF (Industrial

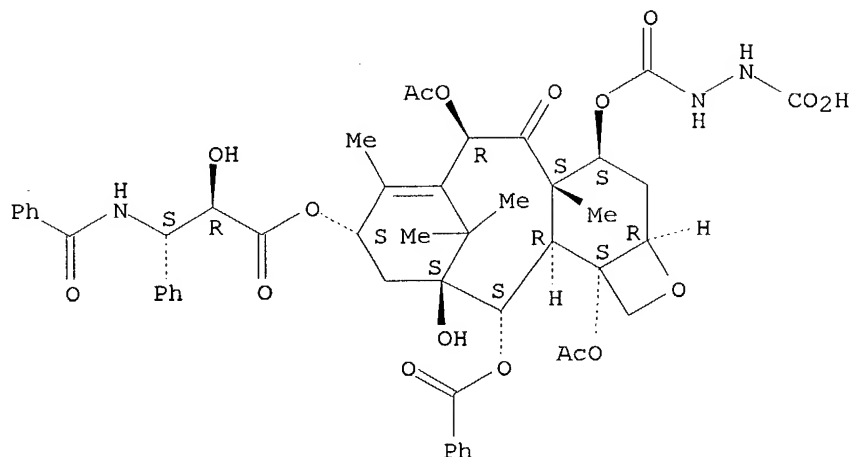
manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (taxol 7-carbazates with improved water-soly. and/or enhanced therapeutic activity)

RN 180965-73-5 CAPLUS

CN 1,2-Hydrazinedicarboxylic acid, mono[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]

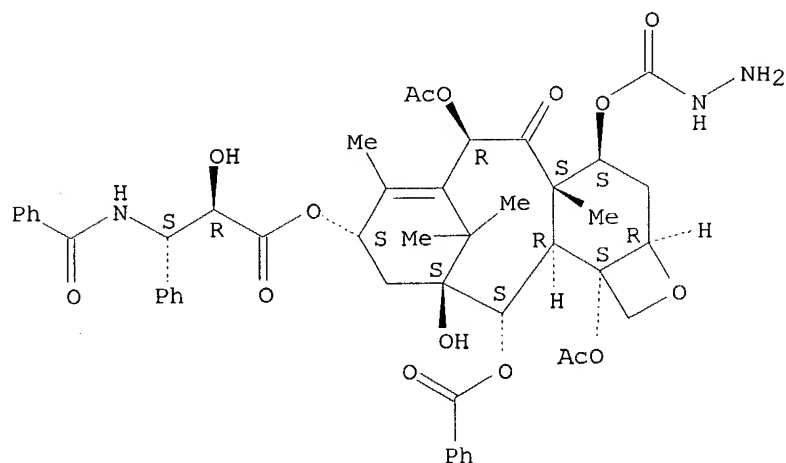
ester,
 [2aR-[2a.alpha., 4.beta., 4a.beta., 6.beta., 9.alpha. (2R*,), 11.alpha.
 ., 12.alpha., 12a.alpha., 12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



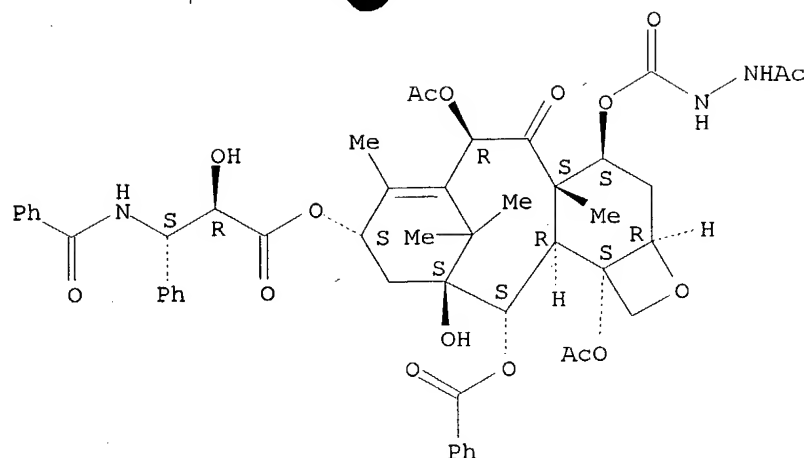
RN 180965-75-7 CAPLUS
 CN Hydrazinecarboxylic acid, 6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl ester,
 [2aR-[2a.alpha., 4.beta., 4a.beta., 6.beta., 9.alpha. (2R*, 3S*), 11.alpha.
 ., 12.alpha., 12a.alpha., 12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180965-76-8 CAPLUS
 CN Hydrazinecarboxylic acid, 2-acetyl-, 6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl ester,
 [2aR-[2a.alpha., 4.beta., 4a.beta., 6.beta., 9.alpha. (2R*, 3S*), 11.alpha.
 ., 12.alpha., 12a.alpha., 12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:434116 CAPLUS

DOCUMENT NUMBER: 125:150894

TITLE: PEG modified anticancer drugs: synthesis and biological activity

AUTHOR(S): Pendri, Annapurna; Gilbert, Carl W.; Soundararajan, Soundara; Bolikal, Durgadas; Shorr, Robert G. L.; Greenwald, Richard B.

CORPORATE SOURCE: Enzon Inc., Piscataway, NJ, 08854, USA

SOURCE: J. Bioact. Compat. Polym. (1996), 11(2), 122-134

CODEN: JBCPEV; ISSN: 0883-9115

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three well known anticancer drugs, doxorubicin, methotrexate and paclitaxel (taxol), have been modified by the permanent attachment of poly(ethylene glycol) (PEG) and evaluated for in vitro cytotoxic activity against murine leukemias P388 and L1210. The relative potencies of the PEG derivs. suggest that modification of antitumor agents with this type of polymer yields compds. that are highly water sol. but less cytotoxic.

IT 161742-50-3

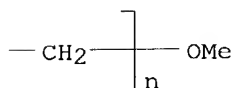
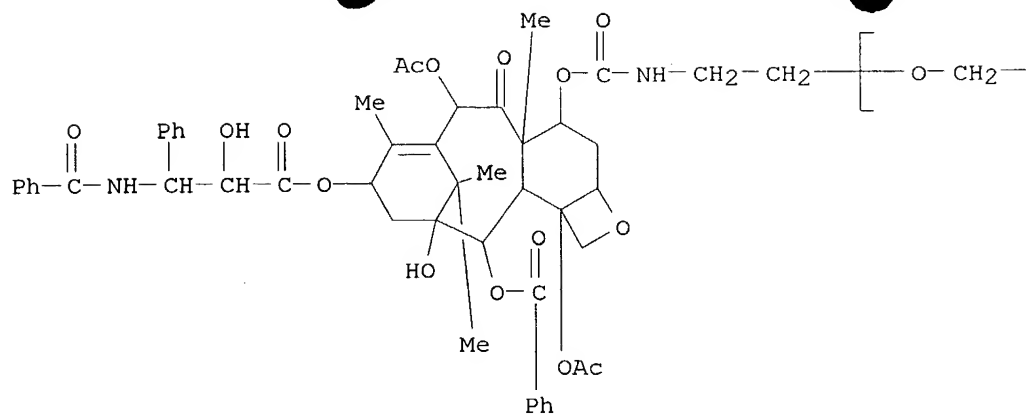
RL: RCT (Reactant)

(soly. and cytotoxicity of PEG-modified anticancer doxorubicin, methotrexate and paclitaxel)

RN 161742-50-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-methoxy-, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)



L3 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:308979 CAPLUS

DOCUMENT NUMBER: 122:214287

TITLE: Highly Water Soluble Taxol Derivatives:

7-Polyethylene

Glycol Carbamates and Carbonates

AUTHOR(S): Greenwald, Richard B.; Pendri, Annapurna; Bolikal, Durgadas

CORPORATE SOURCE: Enzon Inc, Piscataway, NJ, 08854, USA

SOURCE: J. Org. Chem. (1995), 60(2), 331-6

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 122:214287

AB The first examples of highly water sol. taxol derivs. (0.1 mmol/mL) were prepd. by the attachment of polyethylene glycol (mol. wt. 2-5 kD) at the 7-position of taxol via a urethane or carbonate linkage. When lower mol. wt. polyethylene glycols (350 and 750) were used, the solubilities were considerably lower (1.87 .times. 10-3 mmol/mL) but still substantially greater than taxol itself. Addnl. 7-substituted taxol derivs. were also prepd. by utilizing small mols. consisting of sugars and ionic and multifunctional compds. However, most of these derivs. had solubilities, calcd. from HPLC retention times, that did not differ significantly from taxol itself. The use of methoxyacetate as a protecting group during these syntheses is discussed.

IT 161742-50-3P 161742-57-0P 161742-58-1P

161742-59-2P 161742-60-5P 161742-61-6P

161742-62-7P 161742-63-8P 161742-64-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

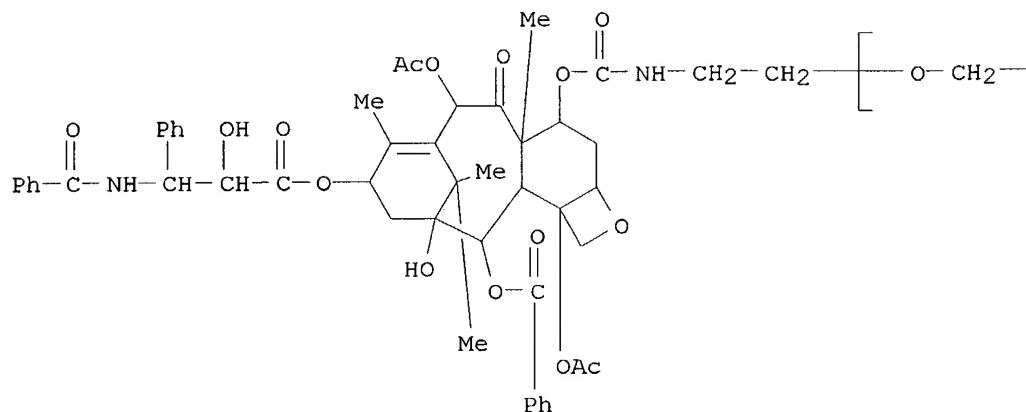
(highly water sol. taxol 7-polyethylene glycol carbamates and carbonates)

RN 161742-50-3 CAPLUS

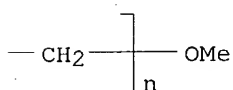
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-methoxy-, [2aR-

[2a.alpha., 4.beta., 4a.beta., 6.beta., 9.alpha. (2R*, 3S*), 12a.alpha., 12b.alpha.]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



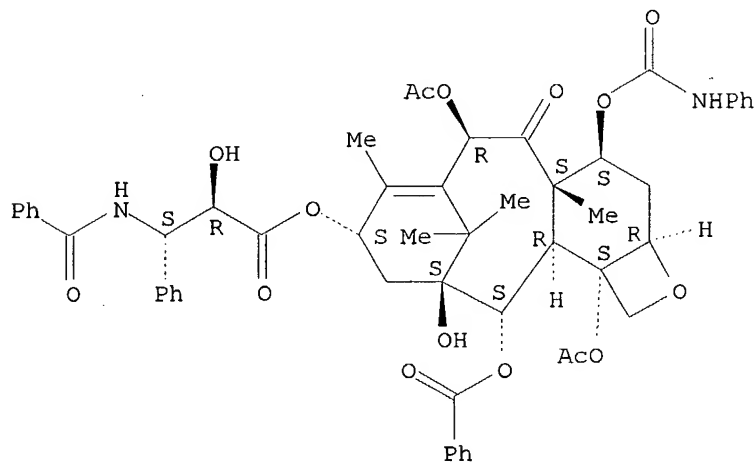
RN 161742-57-0 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-

[[(phenylamino) carbonyl] oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,

[2aR-[2a.alpha., 4.beta., 4a.beta., 6.beta., 9.alpha. (.alpha.R*, .b eta.S*), 11.alpha., 12.alpha., 12a.alpha., 12b.alpha.]]- (9CI) (CA INDEX NAME)

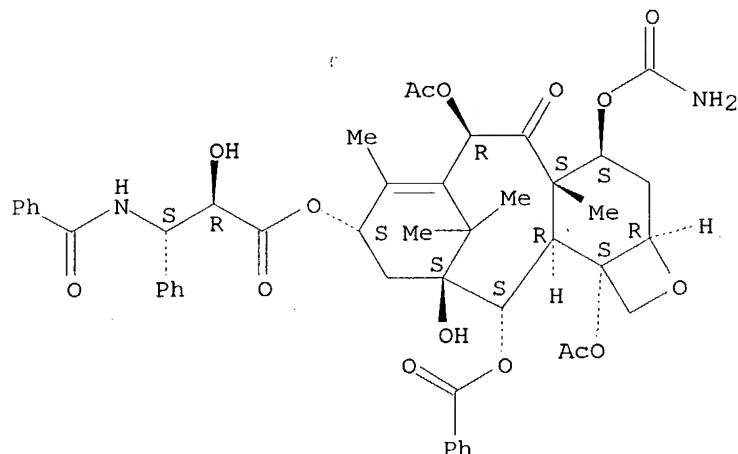
Absolute stereochemistry.



RN 161742-58-1 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-4-[[aminocarbonyl]oxy]-12-(benzoyloxy)-
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S
*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-(9CI) (CA INDEX NAME)

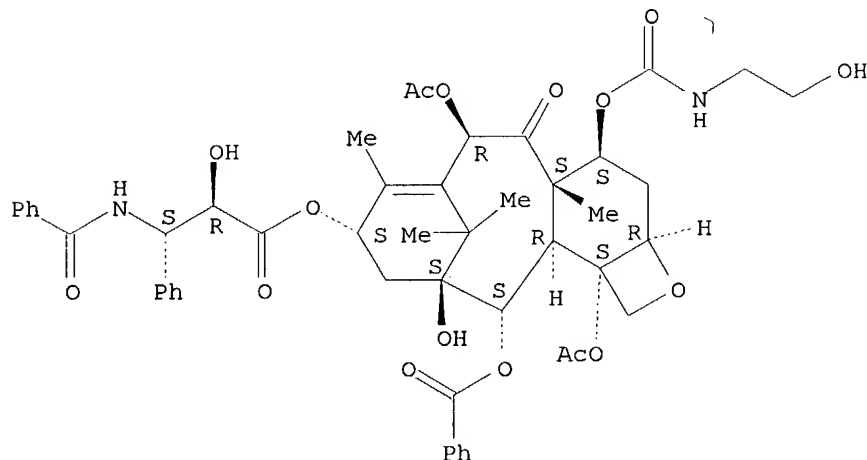
Absolute stereochemistry.



RN 161742-59-2 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4-[[[(2-hydroxyethyl)amino]carbonyl]oxy]-4a,8,13,13-
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
ester,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S
*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 161742-60-5 CAPLUS

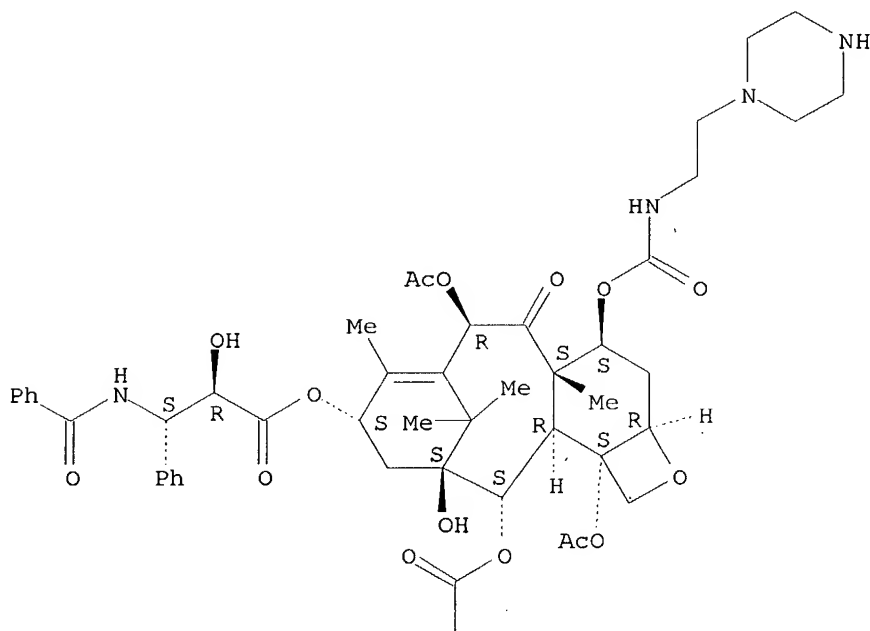
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[[[2-(1-
piperazinyl)ethyl]amino]carbonyl]oxy]-7,11-methano-1H-

cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-

[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

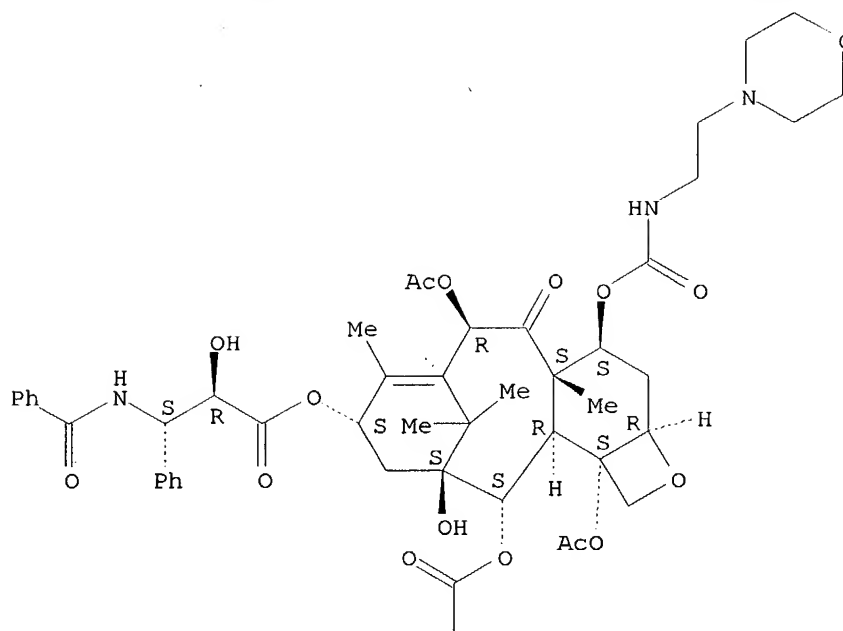
Ph

RN 161742-61-6 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]oxy]-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-

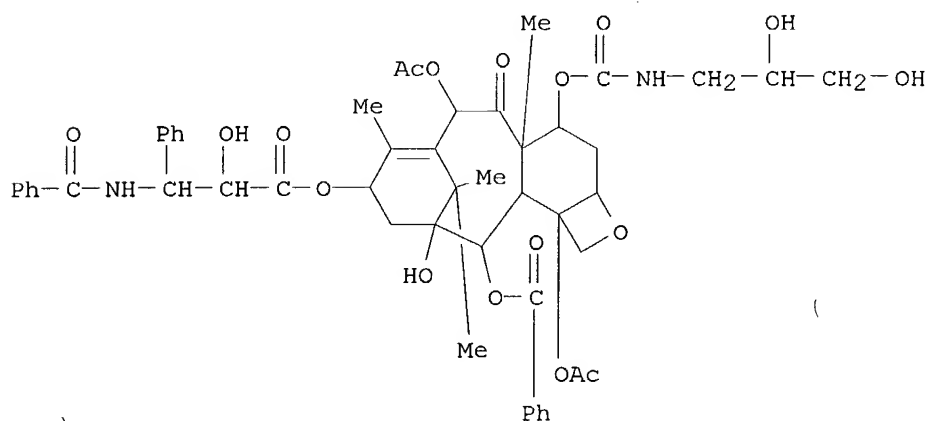
[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Ph

RN 161742-62-7 CAPLUS
 CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(2,3-
 dihydroxypropyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
 dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)



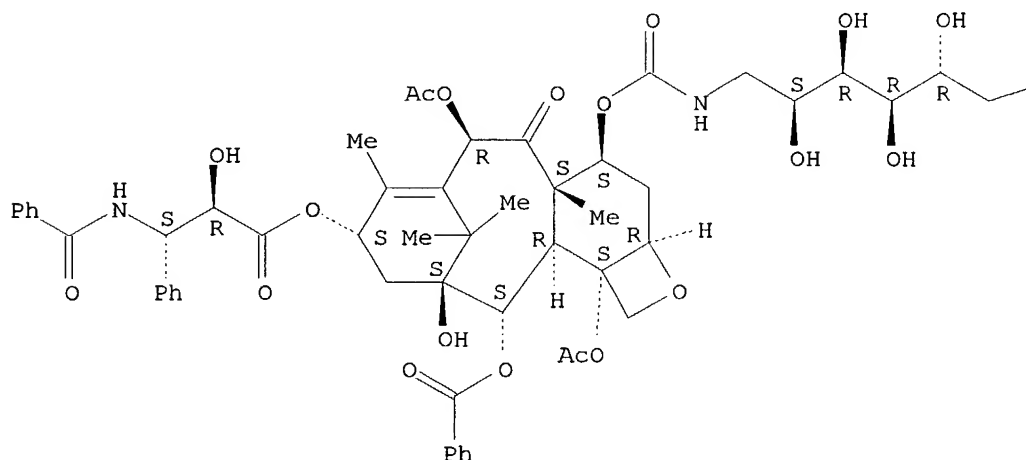
RN 161742-63-8 CAPLUS
 CN D-Glucitol,
 1-[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-
 3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
 dodecahydro-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-

cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]-1-deoxy-,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.
pha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

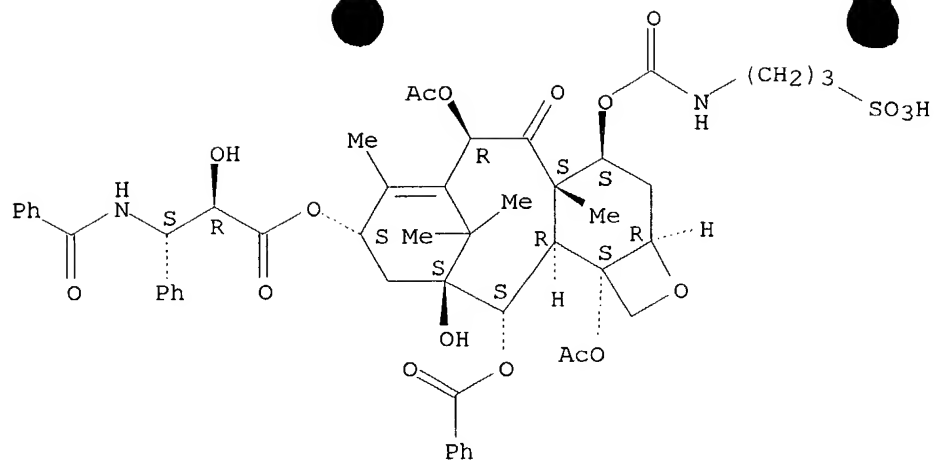
OH

RN 161742-64-9 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,
6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[[[3-
sulfopropyl)amino]carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-
b]oxet-9-yl ester, monosodium salt,
[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.

a.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]
]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

L3 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:139666 CAPLUS

DOCUMENT NUMBER: 122:240034

TITLE: Taxol structure-activity relationships: synthesis and biological evaluation of taxol analogs modified at

C-7

AUTHOR(S): Chen, Shu-Hui; Kant, Joydeep; Mamber, Stephen W.; Roth, Gregory P.; Wei, Jian-Mei; Marshall, Dan; Vyas, Dolatrai M.; Farina, Vittorio

CORPORATE SOURCE: Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492-7660, USA

SOURCE: Bioorg. Med. Chem. Lett. (1994), 4(18), 2223-8
CODEN: BMCLE8; ISSN: 0960-894X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of taxol derivs., modified at C-7, is described. This includes sulfonate, silyl ether, ester, carbonate, carbamate, fluoro, dehydro and deoxy derivs. Biol. evaluation shows that these modifications do not usually significantly compromise activity. However, none of the C-7 analogs prepd. thus far have been shown to be better than taxol in both in vitro and in vivo assays.

IT 162081-16-5P 162081-19-8P 162081-21-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

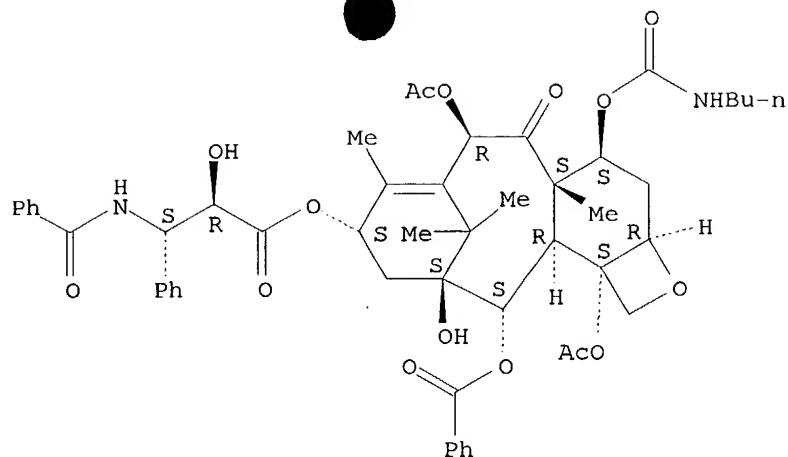
(synthesis and cytotoxicity of taxol analogs modified at C-7)

RN 162081-16-5 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[(butylamino)carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha. (.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



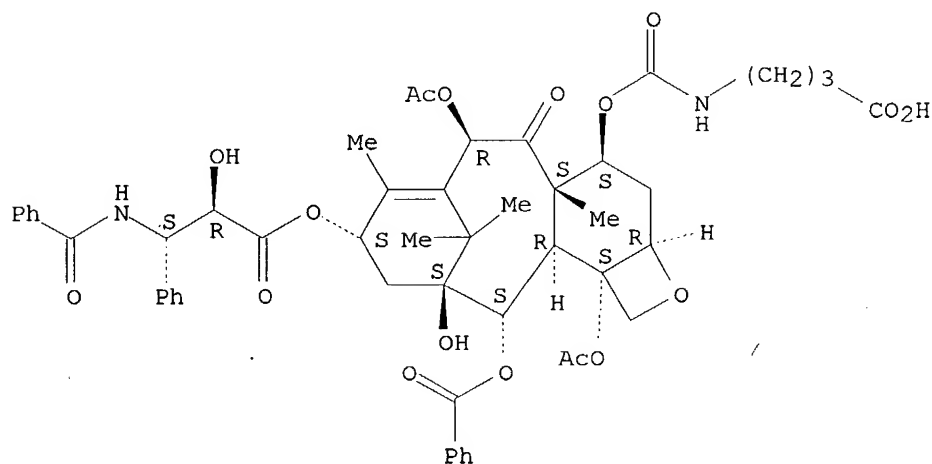
RN 162081-19-8 CAPLUS

CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[(3-carboxypropyl)amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162081-21-2 CAPLUS

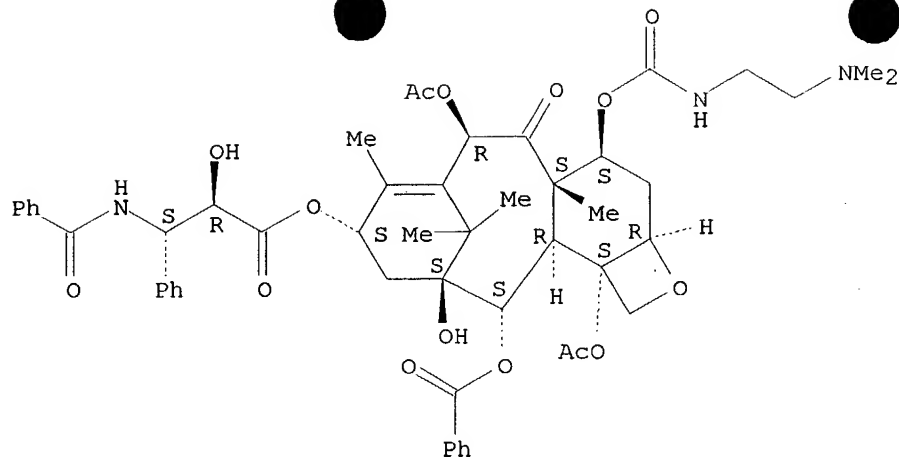
CN Benzenepropanoic acid, .beta.-(benzoylamino)-.alpha.-hydroxy-,

6,12b-bis(acetyloxy)-12-(benzoyloxy)-4-[[[2-(dimethylamino)ethyl]amino]carbonyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-

4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(.alpha.R*,.beta.eta.S*),11.alpha.,12.alpha.,12a.alpha.,12b.alpha.]]-(9CI) (CA INDEX NAME)

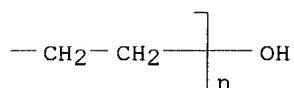
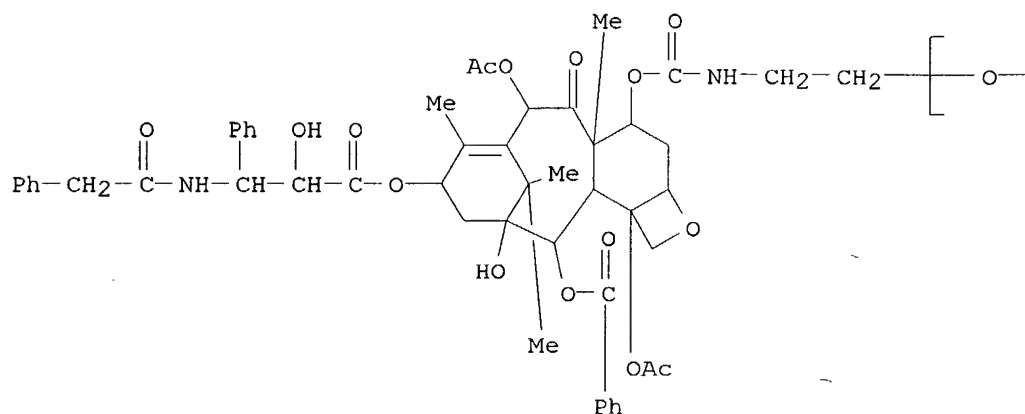
Absolute stereochemistry.



L3 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1994:686601 CAPLUS
 DOCUMENT NUMBER: 121:286601
 TITLE: Taxol-based compositions with enhanced bioactivity
 INVENTOR(S): Greenwald, Richard B.; Shorr, Robert G. L.
 PATENT ASSIGNEE(S): Enzon, Inc., USA
 SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 12
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9420089	A1	19940915	WO 1994-US2441	19940308
W: AU, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9463612	A1	19940926	AU 1994-63612	19940308
PRIORITY APPLN. INFO.:			US 1993-28743	A 19930309
			WO 1994-US2441	W 19940308

OTHER SOURCE(S): MARPAT 121:286601
 AB Taxol-based compns. are disclosed based on the formation of 7-carbamates. In certain aspects of the invention, the compns. include polyethylene glycol and have prolonged circulating lives in mammals, are highly water sol. and substantially non-antigenic. Methods of prepn. and treatment using the compns. are also disclosed. 2'-Acetyl-7-PEG 5000 carbamate taxol (I) was prepd. and tested against various malignant human cell lines and against doxorubicin-sensitive and -resistant mouse lymphoid neoplasms. I was >600 times more sol. in water than the unmodified taxol.
 IT **159022-69-2**
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (taxol-based compds. with enhanced bioactivity and their prepn.)
 RN 159022-69-2 CAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[[6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-9-[2-hydroxy-1-oxo-3-phenyl-3-[(phenylacetyl)amino]propoxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]amino]ethyl]-.omega.-hydroxy-, [2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.,



IT 159022-68-1P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(taxol-based compds. with enhanced bioactivity and their prepn.)

RN 159022-68-1 CAPLUS

CN Glycine, N-[[[6,12b-bis(acetyloxy)-12-(benzoyloxy)-

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-9-[2-hydroxy-1-oxo-3-phenyl-3-[(phenylacetyl)amino]propoxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]-,

[2aR-[2a.alpha.,4.beta.,4a.beta.,6.beta.,9.alpha.(2R*,3S*),11.alpha.,12.alpha.pha.,12a.alpha.,12b.alpha.]]- (9CI) (CA INDEX NAME)

